COLUMBIA LIBRARIES OFFSITE
HEALTH SCIENCES STANDARD
HX64064867
RD651 Ew52 Syllabus of lectures

RECAP

RD651 Ew52

RDG51 Ew52
Columbia University
in the City of New York
College of Physicians and Surgeons

Library

Digitized by the Internet Archive
in 2010 with funding from
Open Knowledge Commons

http://www.archive.org/details/syllabusoflectur00ewin

193

SYLLABUS OF LECTURES

ON

TUMORS.

BY

JAMES EWING, M.D.,

DEPARTMENT OF PATHOLOGY

CORNELL UNIVERSITY MEDICAL COLLEGE.

NEW YORK CITY,

1902.

Columbia University
College of Physicians and Surgeons
Library

RD651
E w52

TUMORS.

Definition. A tumor is an autonomous new growth of tissue.

Scope of Term.

Clinically, any more or less permanent localized swelling is tentatively called a tumor. The pathological classification separates among such swellings.

(1) *Inflammatory Hyperplasias.*
(2) *Retention Cysts.*
(3) *True tumors. Neoplasms.*

(1) Inflammatory Hyperplasia.

It has already been noted that a simple inflammatory process may produce a localized increase in the size of a part, simulating a tumor. Instances of this sort occur especially in the skin and mucous membranes. (*Nasal polyps, fungous endometritis and uterine polyps, chronic prostatitis, venereal warts, fungoid growth following eczema.*)

This increase in the size of the part is referable to moderate increase in the number and size of cells, to retention of secretion, and to inflammatory exudate. Such inflammatory hyperplasia may, however, pass by insensible gradations into a true tumor process, and this fact constitutes one of the strongest arguments against the parasite theory of the origin of tumors.

(2) Retention Cysts.

The retention of secretion in occluded glandular alveoli accounts for much of the bulk of many tumors, but not infrequently such retained secretion produces a marked swelling or tumor apart from any true neoplastic process. It is commonly seen in chronic inflammations of glandular structures. (*Galactocele, one form of goitre, ranula, simple and corpus luteum cysts of ovary, hydronephrosis, congenital cystic kidney?*)

(3) Neoplasms.

This term applies to the autonomous new growths in which the process differs essentially from that of inflammatory hyperplasia, in that the multiplication of cells is much greater and the new cells produced differ in type from the normal cells originating the tumor.

The broadest conception of a tumor and one which perhaps best expresses the relation of a tumor to other pathological processes and to the originating tissue is that of a *parasitic growth.* In this sense a tumor grows for itself and at the expense of the harboring tissue and host. The parasitic relation is apparent in certain monsters where considerable portions of one individual are implanted in another, while there appear to be all gradations between the extreme examples of parasitism, such as the Siamese twins, through the sacral teratomata, dermoids, embryonal tumors of the genito-urinary tract, even to the epithelioma of the lip which is believed by some to originate from misplaced epithelial cells which have taken on an independent and parasitic existence (Cohnheim, Ribbert). This conception of the parasitic nature of tumors is also one of the strongest arguments against the belief that neoplasms are caused by the invasion of the

cells by parasitic microorganisms. Thus it would seem that the tumor itself is the parasite.

Characters of Tumor Cells.

Anaplasia.

Tumor cells are usually less differentiated than their cells of origin. They are usually larger, sometimes smaller, spindle cells may become spheroidal, but whatever the degree of change, tumor cells tend to revert to the less differentiated form of embryonal tissues.

This reversion of the tumor cells to the embryonal type is one of the clearest distinctions between inflammatory and neoplastic processes, and is called *anaplasia.* (Hansemann.)

The nuclei of tumor cells are usually larger than is normal and exhibit an abundance of chromatin, features which indicate greatly increased power of growth. On the other hand tumors of specialized epithelium possess diminished power to produce special secretions. i.e., special power of physiological function. It is believed that one of the essential characters of tumor cells is an excess of the tendency of growth gained at the expense of the capacity for function. (Adami.) This physiological fact should be included in the conception of anaplasia.

Metaplasia.

In some tumors the cells may exhibit distinct differences from their original function.

Thus, fibroblasts produce bone and cartilage, and columnar epithelium becomes flat and round. This change is called *metaplasia.*

Metaplastic changes are not indiscriminate but follow

influences based on the embryological development of tissues.

Fibroblasts may produce bone and cartilage because all of these are closely related mesoblastic tissues; but epithelial cells never assume the characters of fibroblasts in producing bony or cartilaginous tissues.

Cell-division.

Tumor cells multiply by mitosis but instead of always dividing equally into two new cells three or more may be formed with varying quantities of chromatin and protoplasm. Such pathological mitosis increases with the anaplasia and malignancy of the tumor. Amitosis is also, to a less extent, concerned in the multiplication of tumor cells. Endogenous cell formation also occurs.

Structure and Growth of Tumors.

Tumor processes have been shown to originate in one or many very small groups of cells. The tumor may then grow by the multiplication of these cells alone, or other normal cells may be steadily excited to excessive proliferation. Thus in carcinoma of the colon the edges of the growth frequently show all gradations from normal glandular epithelium through pronounced hypertrophy of epithelial cells up to the active tumor cells with excess of chromatin.

The former tendency produces an encapsulated growth, especially if benign, (*lipoma*), or the tumor cells originating from a small focus may rapidly push their way through lymph spaces and grow to a large size in neighboring parts. (*Carcinoma of axillary nodes with minute nodules in breast.*) The latter tendency yields locally spreading growths with or without metastasis. (*Diffuse carcinoma of colon.*)

CLASSES OF TUMORS.

Connective Tissue.

Fibrillar connective tissue	**Fibroma**
Mucous tissue	**Myxoma**
Fat tissue	**Lipoma**
Cartilage	**Chondroma**
Bone	**Osteoma**
Embryonal connective tissue	**Sarcoma**
Endothelium	**Endothelioma**

Muscle Tissue.

Smooth muscle	**Leiomyoma**
Striated muscle	**Rhabdomyoma**

Nerve Tissue.

Nerve cells and fibres	**Neuroma**
Neuroglia	**Glioma**

Vessels.

Blood	**Angeioma**
Lymph	**Lymphangeioma**

Epithelial Tissue.

Glands	**Adenoma**
Epithelium, Glandular	**Carcinoma**
Epithelium, Squamous	**Epithelioma**
Skin	**Dermoid**
Complex Embryonal Implantations	**Teratoma**

FIBROMA.

Occurrence. Subcutaneous tissue, intermuscular septa, breast, and other organs.

Cells of Origin. Usually from fibroblasts of supporting connective tissue. Or from fibroblasts of vessel walls, when many new vessels and much endothelium may accompany the growth. Or from basement membrane-cells of alveoli. (*Canalicular fibroma of breast.*) Or from fibroblasts of nerve trunks.

Structure. That of fibrillated connective tissue. The proportion of cells and fibres varies greatly, the more cellular tumors becoming fibrosarcomatous and recurring locally after operation. They are hard, from densely packed cells and fibres, or soft, from excess of cells and from œdema.

Varieties: Multiple fibroma of skin, arises usually in nerve trunks and shows fibroblasts mingled with much endothelium, and sometimes with nerve fibres.

Keloid is a term applied to very dense acellular fibrous thickenings of scars, with numerous lymph channels, but extending beyond them and following the line of blood channels. It is possibly of inflammatory origin, but is progressive, although not extending beyond the cutis. *Fibrous papilloma* is common on mucous surfaces and consists of fibrous tissue and vessels covered with hypertrophic epithelium. It is often largely inflammatory in origin.

Combinations of fibroma with other tumors are very frequent.

MYXOMA.

Occurrence. In loose connective tissue of back, navel, cheek, vulva, scrotum, mucous surfaces, bone marrow, breast, placental mole, nerve trunks, parotid.

Cells of Origin. Fibroblasts of supporting connective tissue, of basement membranes, of adenoid tissue, of nerve trunks; and fat cells.

Structure. Peculiar polyhedral cells lying in a mucinous matrix which shows precipitated basic fibrils and finely granular or homogeneous mucus. The proportion of cells and mucus varies greatly. The cells are often connected by radiating processes.

Varieties: (1) **Primary myxoma** arises from embryonal mucous tissue which precedes the formation of connective tissue and fat. This tumor is rare.

(2) **Secondary myxoma** is an œdematous fibroma or lipoma which undergoes mucoid degeneration. Such tumors are common. It is usually difficult to distinguish primary from secondary myxomata.

The primary myxoma is seen in the new born; a typical form in the hydatid mole, which is however largely an hydropic degeneration. Clinically the myxoma of the central and peripheral nervous systems is important. Mucous polyps of the nares, etc., are largely inflammatory. Combinations with lipoma and sarcoma are frequent.

LIPOMA.

Occurrence. Skin, often in neck and back, rarely in hairy parts. Fasciæ, joint capsules, renal capsule, muscles (pseudo-hypertrophy), nerves (multiple symmetrical lipomata).

Cells of Origin. Fat cells and fibroblasts.

Structure. That of normal fat tissue, but the tumor cells vary in size, are irregularly grouped into uneven lobules, blood vessels are usually more abundant, and fibrous tissue usually excessive or deficient. Growth is usually circumscribed, but may be diffuse.

Varieties: Combinations are frequent with myxoma, fibroma, angeioma, and sarcoma.

CHONDROMA.

Occurrence. One of the most widely distributed of tumors, arising from (1) cartilage, bone, or connective tissue; (2) forming frequently in other tumors of the connective tissue series, including endothelioma, and (3) very frequently present in tumors developed from misplaced embryonal remnants.

Cells of Origin. Fibroblasts, endothelium, bone and cartilage cells. Embryonal connective tissue cells.

Structure. The type is usually that of hyaline cartilage, but may be fibrous, or fibro-elastic. The cells vary greatly in size, number, and arrangement. The stroma is hyaline,

or fibrous, mucoid, or calcific. Blood vessels are more numerous than in normal cartilage but degeneration and necrosis is common.

Varieties: Combinations with fibroma, osteoma, lipoma, myxoma, and sarcoma, are common. The most peculiar and striking chondromata are those that develop from misplaced embryonal cells, as along the vertebræ, epiphyses, in the genital organs, parotid, and lung.

OSTEOMA.

Occurrence. On bone and periosteum, or in soft tissue as a part or secondary feature of fibroma, chondroma, and sarcoma.

Cells of Origin. Bone or cartilage cells, and fibroblasts.

Structure. Dense ivory osteomata show very few Haversian canals or medullary spaces, while spongy osteomata are more vascular and contain numerous medullary spaces. The structure may be that of bony tissue or the cells may have comparatively few processes, somewhat resembling cartilage cells, and the matrix is less dense than that of bone (osteoid tissue).

Varieties: Inflammatory exostoses are difficult to separate from tumors. Pure osteomata are not common but are most frequent about the cranium.

Osteo-fibroma, chondroma, and sarcoma, are the usual types. Osteoma occurs, rarely, in the brain and lung, from misplaced embryonal tissue. In the jaw one variety is the *odontoma,* containing bone, dentine, and enamel organ.

SARCOMA.

Definition. A sarcoma is a malignant tumor developed from cells of the connective tissue series, and of which the cells are more abundant than in normal connective tissue or in simple benign tumors of connective tissue, while the intercellular substance, although present, is usually very scanty. In these tumors the anaplasia is pronounced.

Occurrence. Sarcomata develop wherever the simple tumors of the connective tissues are found. They are most frequently located in the skin, bones, lymph-nodes, and viscera.

Cells of Origin. The fibroblast and all its derivatives, including cartilage, bone, fat, lymphoid, and smooth muscle cells, and from the fibroblasts of blood vessels, nerve trunks, basement membranes, and interstitial tissues.

Cellular endothelial tumors are closely related to sarcomata.

Structure and Varieties.

(1) Simple Fibroblastic Sarcoma.

(*a*) **Small and large spindle cell sarcomata** contain numerous spindle shaped fibroblasts, with little fibrillated inter-cellular substance, usually with very few blood vessels. Some of these tumors appear to be derived from the fibroblasts or endothelium or embryonal smooth muscle cells of many minute blood vessels, but the cells exhibit the characters of fibroblasts. They are common in the skin where they develop from nerve trunks and basement membranes of sweat or sebaceous glands or hair follicles. There are all gradations from simple fibroma to

fibroblastic sarcoma and numerous combinations with other types of sarcoma.

(*b*) **Giant cell sarcoma** contains large and small giant cells of the type of myeloplacques, many large or small spindle cells, and usually many blood vessels.

Giant cells are most frequently seen in periosteal or medullary sarcoma where they represent the osteoclasts of developing bone or of marrow.

Giant cells also form in sarcomatoid tumors of endothelial origin. They are common in the tumors called perithelioma.

(*c*) **Small round cell sarcoma** is almost always derived from lymphocytes, and is called lymphoma or lympho-sarcoma. Possibly it may at times be of fibroblastic origin.

(2) Lymphoma.

(*a*) **Simple lymphoma** is a tumor of lymph nodes in which the cells are of the usual type of lymphocytes. The tumor growth remains within the distended capsule of the node, the outlines of the follicles are still partly preserved, lymph sinuses are not obliterated, and a reticular stroma is present. This tumor is seen in pseudo-leukemia, and lymphemia.

(*b*) **Lympho-sarcoma** contains small and large lymphocytes or larger cells, the outlines of follicles are indistinguishable, the capsules of the nodes are infiltrated and ruptured, and the sinuses obliterated. Some of the nodes in pseudo-leukemia and lymphemia may be of this type but the best examples are seen as more circumscribed but very malignant tumors of single groups of lymphnodes or of the viscera.

p. 21-28 bound after p. 36

As one passes up the scale of malignancy in lymphoid tumors the cells become larger and eventually fall in the class of large round cell sarcoma.

(*c*) **Large round cell sarcoma** must at present be treated as a heterogeneous group, as the origin of such tumors is not always clear. The group includes, (1) Large round cell tumors of fibroblastic origin. (2) Large round cell lympho-sarcoma. (3) Melano-sarcoma. In all but lympho-sarcoma the cells are apt to be not strictly spheroidal, but polygonal.

(1) Fibroblastic Large Round Celled Sarcoma.

Perithelioma (Telangiectatic sarcoma), a common tumor appears to be the sole example. It is composed of a congeries of blood vessels surrounded by thick sheaths of large round or fusiform cells. The tumor cells radiate out from these vessels. Or, the vessels are lost and the cells diffusely scattered.

The exact origin of this tumor is uncertain but it may be regarded as a derivative of the large epithelioid fibroblasts of the sub-endothelial connective tissue of blood vessels.

(2) Large Round Cell Lympho-sarcoma.

These tumors are most frequently seen in lymph nodes and in the cæcum. They are rapidly growing and are among the most malignant of tumors. *Myeloma,* a large round cell tumor developing from certain cells of bone marrow, may be classed here.

The structure includes the cells, and a supporting framework of reticular connective tissue, with small blood vessels. The cells include a small proportion of lymphocytes, a majority of large mononuclear cells, and

In well nourished tumors the multiplication of cells may be equally active in all parts (*central growth*).

Frequently the nutrition is deficient in the central parts of a tumor and growth is most active or exclusively located in the peripheral portions (*peripheral growth*).

Some tumors consist exclusively of new cells of a single type, but most new growths contain, besides the specific tumor cell, nerves, blood vessels, and a supporting frame work of connective tissue. In carcinoma there is often an excessive amount of new connective tissue, usually as the result of productive inflammation. The new blood vessels in tumors may be the result of productive inflammation, or the tumor cells when arising from cells of vessel walls may persist in their normal functions and produce many neoplastic vessels. Several varieties of tissue arising from embryonal remnants of the same type are found in the mixed tumors or teratomata.

Degenerative Processes.

Hydropic, mucoid, hyaline, glycogenic, and fatty degeneration, are commonly observed in tumors, necrosis is a frequent result of imperfect blood supply, and inflammatory processes occur as in normal tissues. These changes tend to limit the growth of tumors by diminishing the number of proliferating cells. (*Gelatinous carcinoma.*)

The growth of tumors is usually much more active than that of the tissue originating them. The blood supply must therefore be correspondingly large, and indeed the demands for nutrition of some tumors may cause atrophy of the other tissues of the body. (*Lipoma in thin subjects; large sarcomata.*)

Function in Tumor Tissue.

Tumor tissue usually retains some of the function of the original tissue; sometimes this function is exaggerated in the tumor, and usually it is perverted while not inhibited.

Thus, the adenomatous thyroid protects against the myxœdema which follows total extirpation of the thyroid; there may be milk in the cysts of adenoma of the breast, urine in adenomatous alveoli of the kidney, bile in metastatic carcinoma from the liver, and many tumors of mucous surfaces secrete an excess of mucus.

Metastasis.

Tumor cells when detached from one another are still more or less capable of growing. Such detached cells are often carried by the lymph stream, less often by the blood, to distant parts where they lodge and develop into metastatic tumors. Vascular tumors and those which tend to grow into lymph spaces most frequently develop metastases and are therefore most malignant. In many tumors the paths and locations of metastases are very characteristic. Usually metastases are located in the nearest lymph nodes, but sometimes early metastases are far distant from the original tumor. (*Secondary growth over scapula from cancer of stomach.*) Numerous instances of *retrograde metastasis* have been recorded. (*In pelvic lymph nodes from cancer of liver.*) A favorite seat of metastasis for carcinoma is the bone marrow.

Malignancy of Tumors.

Evidences of malignancy may be *clinical* as (1) rapid growth, (2) pain and ulceration, (3) involvement of ad-

jacent tissues, (4) local recurrence, (5) metastases, (6) cachexia.

Histological evidences of malignancy include:

(1) Markedly cellular character.

(2) Relatively large size of cells and abundance of chromatin.

(3) Abundance of mitotic nuclei.

(4) Abnormal arrangement of cells.

(5) Tendency to invade neighboring tissues.

The first three of these histological features are really the means of estimating the grade of anaplasia which is therefore the criterion of malignancy. The sole feature of malignancy of a tumor may be an unfortunate position where it endangers vital structures, or its large size, or it may be capable merely of local recurrence, or it may possess all the elements of malignancy. The prognosis varies in each instance. The estimation of the malignancy of tumors requires an intimate knowledge of both their clinical and their histological characters.

ETIOLOGY OF TUMORS.

(a) General.

Age and sex determine largely the types and locations of tumors. There is a very slight hereditary predisposition affecting the occurrence and type of tumors.

(b) Local.

Trauma is frequently concerned with the development of tumors, (*epithelioma of lip; sarcoma after fractures of bones*). Local malformations, as nævi of the skin, misplaced portions of adrenal or thyroid, are frequent starting points of tumors.

(c) Exciting Cause.

The exciting cause of tumor growth is not known, and several theories regarding its origin are maintained.

(1) Cohnheim's Theory of Embryonal Remnants.

Cohnheim believes that tumors develop from:

(1) Masses of complex or simple tissue misplaced during embryonal development, yielding the mixed tumors or teratomata.

(2) Small groups of embryonal cells, (*a*) misplaced or (*b*) not misplaced, which have failed to reach their full differentiation into specific tissues.

The immediate exciting cause of the sudden growth of these cells is *increased nutrition and irritation.* Tumors therefore frequently develop in the breast and uterus which pass through many physiological changes in activity.

Roux found 1-13 minute foci of cells misplaced from other layers in the entoderm of frogs' embryos, and Barfurth produced dermoids by puncturing ova in the gastrula stage, thereby misplacing cells.

In order to elucidate the obscure nature of the inception of a tumor process in these misplaced cells, the idea of a **disturbance in tissue tension** has been suggested.

The idea of tissue tension involves

(*a*) Mechanical pressure of cells on each other, (*b*) the distribution of nutriment among the cells, and (*c*) the acquired demands on the cells for specialized function instead of on their embryonal habit of simple multiplication. Tissue growth normally ends when the regenerative capacities of cells are restrained by tissue tension. Embryonal remnants being cut out of this circle of influences are liable to resume their embryonal capacities of multiplication and feeling no restraint of neighboring

cells and no demands for specialized function go to develop tumors.

Scores of examples illustrate the partial truth of Cohnheim's theory: adrenal tumors of kidney; rhabdomyoma of kidney, genito-urinary organs, breast and heart; embryoid tumors of ovaries, uterus, vagina; adenomyoma of uterus; adenoma of supernumerary breast, thyroglossal duct; chondroma of parotid from misplaced cartilage from the ear; epithelioma from branchial clefts; glio-adenoma from misplaced vertricular remnants in brain; cholesteatoma of skull; osteoma of lung; peritoneal epithelial cysts in spleen; and the entire group of dermoids and teratomata.

In fact in every organ are well recognized types of tumors certainly developing from embryonal remnants.

Such tumors producing a tissue differing from that of the harboring organ are called **heterologous.**

Cohnheim's theory embodies one of the great facts in the etiology of tumors and is very likely a complete explanation of the group of heterologous tumors.

It is equally certain that all tumors, especially most carcinomata, fibromata, sarcomata, of simple structure homologous with that of the harboring organ, are not derived from embryonal cells. At any rate there are no means of identifying such cells, in the breast for instance, and such a theory therefore appears not to admit of proof for all tumors.

Ribbert's Theory.

Ribbert endeavors to extend Cohnheim's principle to the development of tumors from groups of *adult cells* which by various means lose their relations to their neighbors and thus fail to feel the restraining effects of tissue tension. He does not believe that the development of tumors requires any greater proliferative tendencies than are to

be found in adult cells, which exhibit constant or intermittent powers of multiplication, as in the breast and uterus where malignant tumors are common. The initial separation of the cells from the influence of the tissue tension he refers to *the growth of new connective tissue of inflammatory origin into the epithelial layer,* and he describes such fibroblasts between groups of epithelial cells in psoriasis of the tongue with early epithelioma and in an adeno-carcinoma of the stomach.

This theory accords with many facts known in regard to the origin of homologous tumors; with the frequent development of carcinoma in chronically irritated tissues, as epithelioma of muco-cutaneous junctions, adenomata of liver from ducts snared off in cirrhosis; adenoma of kidney in old nephritis; epithelioma following lupus; multiple chondromata of epiphyseal lines in the irregular ossification of rickets; carcinomata after crushing injuries; syncytioma from misplaced chorionic cells, etc.

It is rather a matter of wonder, if one accepts this theory, that tumors are not vastly more common, as misplacement of adult cells must be frequent, and Ribbert's theory somewhat inadequately defines the particular forces precipitating the misplaced cells into the malignant tumor process. Numerous very painstaking attempts to produce tumors experimentally by separating without destroying tissue cells have failed. Some other factor appears to be needed.

The principles involved in Cohnheim's and Ribbert's theories represent the most mature judgment of the problem of tumors, probably reach as near the complete explanation as is at present possible, and separate the tumor process distinctly from parasitic disease.

Theory of Parasitic Origin of Tumors.

The possibility of a parasitic origin of tumors seems

to be inadmissible for the group of teratomata and it may be said that the above considerations render unlikely such an origin for the usual varieties of homologous tumors. The parasitic theory is applied by its adherents principally to the simple malignant tumors, carcinoma and sarcoma.

Are Microorganisms Present in Tumors?

Many observers have described in the cells of the growing edges of carcinoma and sarcoma peculiar bodies which they believe to be parasites.

The bodies are rounded, homogeneous, and refractive, in the fresh condition sometimes slightly amœboid, 1-15 μ in diameter, surrounded by a clear halo and sometimes by a membrane, sometimes exhibiting a nucleus, often showing bud-like processes, in staining reaction sometimes acidophile sometimes basophile (*Cancer bodies, Plimmer's bodies, Russell's fuchsin bodies*).

These "cancer bodies" are regarded by the adherents of the parasitic theory as (1) blastomycetes or (2) protozoa; and by the great majority of observers as (1) cell inclusions, of a variety of types, but not parasitic, (2) centrosomes, (3) extruded nucleoli, (4) products of cytoplasmic or nuclear degeneration. The great variety of these bodies, their inconstancy and variability of occurrence in tumors, and their presence in other conditions, speak against their parasitic nature.

Relation of Blastomycetes and Protozoa to Cancer.

In a few cases blastomycetes have been cultivated from cancer but the vast majority of attempts have failed and most tumors appear not to contain them.

Attempts to produce timors by inoculation with blastomycetes obtained from tumors or from other sources have

invariably failed. The results of such inoculations have always been purely inflammatory.

It must be concluded therefore that although blastomycetes are occasionally present in cancer their presence is accidental and they are not the cause of the disease.

Protozoa have not been demonstrated in malignant tumors, although it is possible that some of the bodies described as such are really protozoa.

Transplantation of Tumors.

If tumors contain a parasite it is reasonable to expect that the transplantation of a portion of the growth from one animal to another of the same species would be successful. Of many thousand such experiments only two or three have been partially successful, and even in these cases the resulting growth was transitory and of doubtful nature.

CLASSIFICATION OF TUMORS.

Tumors are classified in order to display their relation to each other, and to furnish a basis for uniform nomenclature.

At present these objects are best attained by naming and classifying tumors as we name their adult cells of origin, or the tissue which the tumor most resembles.

The endeavors to create and introduce a classification of tumors based on the ultimate embryological relations of the originating cells have not been successful and are not to be encouraged. Embryological relations have much influence in determining the type and structure of tumors, but the habits of tumor cells are much more often determined by the late acquired habits of the cells than by their early embryological tendencies.

tation, producing the papillary cystic adenomata, which are common in the ovary and kidney.

Such tumors are usually circumscribed and pedunculated, since the hyperplasia may begin in and be limited to very few alveoli, possibly even to a single alveolus. (White.) Considerable anaplasia usually marks the cells of these tumors, but hypersecretion is also common. The membrana propria remains intact, and the supporting connective tissue is usually abundant and vascular.

(3) **Malignant adenoma.** Adenoma sometimes proves malignant while its structure rigidly observes the type of simple adenoma (e.g., *adenoma of stomach*). Usually the malignant qualities of local recurrence, infiltration, or metastasis, are associated with marked anaplasia of cells, which increase in size, especially of the nuclei, and multiply rapidly, increasing the depth of the epithelial lining of the alveolus. Such alveoli push their way through fibrous or muscular tissue, and breaking through the membrana propria, they invade lymphatics and develop metastases.

In such metastases anaplasia may increase or diminish, but the strong tendencies of the cells to assume the orderly alevolar arrangement, while exhibiting the other qualitie of carcinoma, justifies for many of them the term *adeno-carcinoma.* Common examples of malignant adenoma are seen in the gastro-intestinal tract, and uterus. In the ovary they are often of the papillary cystic type. In general it may be said that adenoma of the gastro-intestinal tract and uterus are usually malignant.

CARCINOMA.

Definition. Carcinoma is a malignant tumor of glandular epithelium.

Structure. Carcinoma is distinguished from adenoma, by the greater anaplasia of the cells, their more rapid growth, and their failure to remain within the confines of a more or less specialized membrana propria.

It is seldom that a carcinoma maintains a uniform structure in all its parts, or in all stages of its growth. Not only are minor variations commonly seen in the same growth, but frequently distinctly different types of growth may be observed in the different parts of the original tumor, while in metastasis the structure may be totally at variance with that of the main tumor.

Characters of Cells.

In all types of carcinoma the anaplasia of the cells is distinct. The cells are usually of increased size, their nuclei show an abundance of chromatin, and mitotic figures are numerous in rapid cases.

The shape of the cells is determined sometimes by their natural tendencies, but very often by the local conditions of nutrition and pressure. The cells show abnormal and usually diminished functional capacity. They are subject to various degenerations, fatty, hydropic, mucoid, hyaline, glycogenic. Advanced mucinous degeneration gives the tumor a swollen, elastic, gelatinous appearance, to which the term **gelatinous carcinoma** is applied. This change tends to limit the growth.

The tumor exerts an irritation on the invaded tissues with reactive inflammation of exudative or productive type, which tends partially to limit the advance of the growth.

Sometimes the new fibrous tissue is excessive in amount and of neoplastic type, as in **fibro-carcinoma**, or of acellular type as in **scirrhus.**

Mucous degeneration of the connective tissue, if prominent, is designated by the term **myxomatous carcinoma.**

Carcinomata of exposed surfaces frequently ulcerate, owing to traumatism of the poorly nourished tumor tissue, and various secondary inflammations may result from infection by microorganisms, including pyogenic bacteria, *bac. tuberculosis,* or blastomycetes.

Classification of Carcinomata.

On general histological structure carcinomata may be divided into three classes, **adeno-carcinoma, alveolar carcinoma,** and **diffuse carcinoma.** While the employment of these terms may indicate the general structure of a carcinoma and may thus serve a useful purpose, there is a growing tendency to name and classify these and other tumors according to their exact cell of origin, so far as that can be determined, since it appears that the structure of such accurately defined tumors is nearly always the same.

Varieties.

(1) **Adeno-carcinoma.**

This type of growth is chiefly seen in those situations where malignant adenoma occurs, as in the gastro-intestinal and uterine mucosæ.

The cells are arranged in groups which maintain a somewhat orderly alveolar arrangement and central lumen. In one variety the carcinomatous process develops extensively within the distended alveoli of papillary and cystic adenomata.

Most adeno-carcinomata represent transitional stages

between malignant adenoma and alveolar or diffuse carcinoma. Or a tumor may begin as adeno-carcinoma and maintain that type throughout, even in distant and late metastases.

(2) **Alveolar Carcinoma, (Medullary.)**

This is the most frequent type of carcinoma and occurs in many organs, most often in the breast.

The cells appear in groups confined by the borders of tissue spaces, or walls of vessels, but they are not attached to these walls as to a basement membrane, and they do not preserve a central lumen.

(3) **Diffuse Carcinoma.**

When the growth of cells is very rapid and profuse, little or no subdivision into orderly groups may exist and the term diffuse carcinoma may be applied. This structure is seen in many very cellular tumors, which are rapidly growing, very malignant, and never show any tendency to observe the alveolar arrangement; or the diffuse quality of the growth may result from the absence of supporting tissue, as in a lymph node or blood vessel; or there may be a diffuse infiltration of an organ or tissue by cells appearing singly or arranged in rows, but not in alveoli.

TUMORS DERIVED FROM STRATIFIED SQUAMOUS EPITHELIUM.

These growths form two distinct classes:

(1) *Epithelial Papilloma.* (2) *Epithelioma.*

(1) Papilloma.

Definition. Epithelial papilloma is a tumor in which the growth of epithelium is outward and papillary projections are formed on the affected surface.

There are many transitional phases between inflammatory hyperplasia of squamous epithelium and neoplastic hyperplasia, which it is difficult to distinguish. The venereal wart is an inflammatory hyperplasia; eczema and psoriasis exhibit a uniform inflammatory hyperplasia of the prickle-cell layer; while the ordinary wart, and the papillomas of the bladder and larynx are examples of a true benign tumor of stratified epithelium.

(2) Epithelioma.

Definition. An epithelioma is a malignant tumor derived from stratified squamous epithelium.

Origin and Structure. The tumors derived from the so-called transitional epithelium, as in the bladder, are included in this class. All epitheliomata are derived from

the deeper layers of cells, but while in some (*acanthomata*), the cells assume the pavement type, in others they never progress in their natural development, but remain small and fail to exhibit the pavement type, or develop prickles, or hornification.

There are several inflammatory conditions characterized by a simple hypertrophy of the basal layers of stratified squamous epithelium, as in eczema and psoriasis, and sometimes hypertrophied papillæ project distinctly into the connective tissue, but in epithelioma the growth of cells is more active and there is progressive invasion of the derma or submucosa by masses of cells of neoplastic type.

The variety of structure in tumors of stratified squamous epithelium is very extensive and depends upon (1) the particular cell form giving origin to the tumor, and (2) the grade of anaplasia of the cells. No other tissue is capable of yielding such a multiplicity of tumor-cell forms.

Varieties.

(1) **Prickle-cell Epithelioma. (Acanthoma.)**

In one very distinct class of epithelioma the cells are derived from the prickle-cell layer, and they retain their original flat pavement character, with prickles, and tendency to hornification.

In such tumors the prickle cells are readily identified, the pavement tendencies give rise to concentric masses of cells, often with hornified centres, called epithelial "pearls."

Such tumors frequently develop in the skin, at muco-cutaneous junctions, and in mucous membranes, and they constitute the most numerous class of epithelioma. Their malignancy depends on their situation and degree of anaplasia. In the skin they are less malignant

than in the mucous membranes, but all are characterized by tendency to local recurrence, early ulceration, and metastasis in the lymph nodes.

In the metastases the same histological characters are usually maintained, but the prickles are the first features to be lost. Occasionally, in the original growth the prickles are partly lost, the cell bodies become more granular, the cells are arranged in narrow anastomosing cords, and the term *tubular epithelioma* is sometimes applied.

(2) **Reticulated Epithelioma.**

This tumor occurs in the skin, in two rather distinct forms. (1) The cells are small, cuboidal or fusiform, and densely packed in small or larger masses in the lymph spaces of the derma. These masses are connected by thinner cords of cells, giving to the growth on section a peculiar reticulated appearance. **Rodent ulcer** is such a reticulated epithelioma with large compact masses of cells and usually with ulceration of the surface.

The above masses of cells may undergo liquefaction in one of several foci, with dilatation of inclosed spaces. An *alveolar appearance* is thus formed and the tumor is called **adenoid cystic epithelioma.**

These tumors possess only slight malignancy, very seldom involving adjacent lymph nodes.

(3) **Papillary and Flexiform Epithelioma.**

A frequent form of epithelioma arising from mucous surfaces is composed of thick convoluted layers of epithelium irregularly twisted and supported by a variable amount of connective tissue. Sometimes this connective tissue is abundant, in which case the identity of the convoluted layers of epithelium is distinct. Sometimes the connective tissue is reduced to a very thin covering

of blood vessels and nearly the entire bulk of the tumor is composed of a more or less diffuse mass of epithelial cells in which run numerous thin walled blood vessels. In either case the cells usually lack prickles, always fail to show hornification, and frequently become compressed into fusiform shapes.

These tumors show marked local malignancy and cause wide metastasis.

(4) Epithelioma of Atypcal Cell Type.

In a considerable number of tumors arising from squamous epithelium there is extreme anaplasia of the cells, which combined with the local effects of pressure, produce very atypical cell forms. In these tumors the cells always lack prickles and hornification. They are usually short and fusiform, but they may become considerably elongated. They are usually packed side by side, in dense masses. They are usually well separated from the surrounding connective tissue, if that tissue is adult, but if it is œdematous or cellular the epithelial cells may pass insensibly into the connective tissue.

In the metastases of these tumors the fusiform shape may reappear or the cells may revert to the large pavement type.

The melanoma of epithelial origin illustrates all of these phases, and the epithelioma of the *cervix uteri* may exhibit many of them.

Syncytioma Malignum. Deciduoma.

Definition. Syncytioma is a malignant tumor arising from the epithelium of the chorionic villi.

Structure. The chorionic epithelium is composed of two layers: (1) an outer mass of fused cell protoplasm with

occasionally some giant cells. Hemorrhage, necrosis, ulceration, and metastasis are common.

(3) Melanoma. It is sometimes difficult to distinguish individual examples of round cell tumors of endothelial or epithelial origin, from large round cell sarcoma. This difficulty is encountered in the group called true **melanosarcoma.** These tumors arise in the skin and choroid, may long remain more or less quiescent, and may suddenly, as after incomplete removal, exhibit rapid growth and widespread metastasis.

Two views are held regarding their origin: (1) They are all epitheliomas derived from the downward growth of palisade cells of the Malpighian layer (Unna); or, (2) they are all endotheliomata derived from the lining cells of minute capillaries or lymph spaces of the *rete.* Many of them are certainly epitheliomata, and some are probably endotheliomata. These conflicting views have led some to use the term *melanoma.*

The pigment is developed by large branching cells, *chromatophores,* which accompany the metastases.

ENDOTHELIOMA.

Definition. A tumor developing from the lining cells of lymph or blood vessels or of serous surfaces.

Structure. It is usually cellular, and the cells long retain their endothelial characters, with vesicular nuclei, nucleoli, homogeneous cytoplasm, and condensed cell-borders. They may form pearls, sometimes with calcified centres. Endothelial cells are less sharply separated from

supporting connective tissue than are epithelial cells. Their relation to fibroblasts is seen in the frequent transformation of endothelial tumors into fibrous growths, less frequently into mucous, or, possibly, cartilaginous tissue.

Histological varieties are very numerous.

(1) **Perivascular Endothelioma.**

This type is seen principally in slowly growing multiple tumors of the dura mater. The cells are spindle shaped with rather homogeneous cytoplasm and dense cell borders. The unit of the tumor is a small blood vessel surrounded by 10-15 concentric layers of these cells.

Common variations of this tumor are, diffuse growth of spindle cells resembling fibro-sarcoma, hyaline transformation of considerable areas, and calcification of small foci of cells (*endothelial pearls, psammoma*).

(2) **Interfascicular Endothelioma.**

This tumor occurs in the parotid and other glands, and in the derma. It is derived from a multiplication of the lining cells of lymph spaces, and in the early stages the lumen of the space remains pervious. Or the cells continue to proliferate and close the lumen. The intervening stroma often undergoes hyaline degeneration producing a peculiar appearance sometimes designated as *cylindroma.* Or the tumor may combine with proliferating fibroblasts to produce cartilage. (*Chondro-endothelioma.*)

(3) **Alveolar Endothelioma.**

When the proliferating cells of lymph spaces multiply extensively, a cellular tumor results composed of groups of cells in alveolar arrangement supported by thin bands

of connective tissue resembling the membrana propria of glands.

Such tumors are seen in the parotid, antrum of Highmore, kidney, ovary, etc.

The central lumen may persist or in the masses of cells small secondary lumina or spaces form filled with mucus or other fluids. The cells may retain the characters of endothelia or may be small and cuboidal or become distinctly columnar.

(4) **Angeio-endothelioma. ("Angeio-sarcoma.")**

In this type the cells of blood or lymph vessels multiply while the lumen of the vessel and its circulating contents are fully maintained, yielding vascular tumors of which the unit is a vessel walled by two or more rows of cuboidal endothelial cells.

Sometimes the vessel is lined by very numerous parallel rows of cells. Sometimes the lumen is dilated, and the tumor resembles papillary epithelioma (endothelioma of bone). In these tumors there is little growth of connective tissue.

(5) **Endothelioma of Serous Membranes.**

This tumor is most common in the pleura, where it may develop considerable bulk of new fragile tissue distending the pleural cavity or it may invade the lung through lymph vessels. The superficial growths, even when of large bulk, exhibit a large alveolar structure with cuboidal or columnar cells and little interstitial tissue.

When invading the lung the cells appear in groups distending the tissue spaces and recalling the structure of carcinoma.

Endothelioma of the peritoneum is very rare. It is composed of large flat cells which tend to retain their endothelial characters in secondary and metastatic growths.

MYOMA.

Definition. A myoma is a tumor of muscle tissue.

Structure. These tumors are of two varieties:

(1) Leiomyoma, composed of smooth muscle cells.
(2) Rhabdomyoma, composed of striated muscle cells.
Both varieties contain also a supporting framework of connective tissue often of neoplastic type, and blood vessels.

(1) **Leiomyoma.** The commonest example of this tumor is the uterine fibro-myoma. It is seen also in the intestinal wall, and viscera, and is often multiple. The cells are long spindles with long oval nuclei. They may be distinguished from fibroblastic tumor cells by (1) their greater affinity for eosin and (2) the presence of nuclei within the fibres on cross section; while (3) their arrangement in fascicles is characteristic.

(3) **Rhabdomyoma** is a rare tumor seen in the breast, heart, or genito-urinary organs. The cells vary greatly in size and development, but are identified by their cross striation. Rhabdomyoma is usually a mixed tumor, teratoma, and contains several varieties of tissue. It may exhibit local recurrence after removal but seldom any other grade of malignancy.

TUMORS OF NERVE-TISSUE.

Definition. There are two varieties:

(1) **Ganglionic or true Neuroma** is composed of ganglion cells and their fibres, and glia cells. (2) **Glioma** is composed of glia cells.

Structure. (1) *Ganglionic neuromata* occur in the brain and in various mixed tumors (teratomata) of the ovary, testis, sacral region, and adrenal. They are identified on the presence of poorly developed ganglion cells supported by glia and nerve fibres, and blood vessels. They are rare.

(2) *Glioma* is common in the brain. It is composed of glia cells with many hair-like processes. Blood vessels are numerous and hemorrhages common.

In the retinal glioma the cells are very numerous, processes deficient, and the tumor somewhat resembles lympho-sarcoma.

False Neuroma is a term applied to certain tumors developing in nerve trunks. They are usually multiple and often as cellular as sarcoma, and are found in the skin or along peripheral nerve trunks. In the early stages the cells are large flat endothelia, later they become fusiform and resemble fibroblasts, and by regressive changes the tumor may become largely fibrous. The arrangement of the cells in whorls is characteristic.

ANGEIOMA.

Definition. Angeioma is a tumor composed largely of blood vessels (Hemangeioma) or lymph vessels (Lymphangeioma).

(1) **Hemangeioma.** (*a*) **Simple Angeioma.** This is a common tumor of the skin, where it is called *vascular nævus.* It occurs less frequently in mucous membranes and bone, and it sometimes involves all the soft tissues of an entire extremity, especially in young children.

It consists of a congeries of small or capillary blood vessels, preexisting or new formed, whose walls usually contain an excess of endothelia and fibroblasts, while the supporting connective tissue is also cellular. There are numerous gradations up to angeio-endothelioma, and one of these in which the new vessels are very numerous and of small size with excess of endothelia is called *angioma simplex hypertrophicum.*

(*b*) **Cavernous angeioma** occurs in the skin or viscera, and is composed of circumscribed masses of widely dilated blood spaces supported by trabeculæ of connective tissue.

(2) **Lymphangeioma** is a tumor, usually congenital, sometimes acquired, composed of dilated lymph channels, supported by thin fibrous or fibro-muscular walls. It occurs in the skin, tongue (*macroglossia*), and subserous tissues. The contents of the lymph spaces are clear and watery or milky. *Keloid* is a fibro-lymphangeioma of the skin. *Lymph scrotum* is a mechanical or inflammatory dilatation of the lymphatics of the scrotum, seen in filariasis, and is a result of occlusion of lymphatics by scars.

ADENOMA.

Definition. Adenoma is a tumor composed of glandular epithelial cells maintained more or less perfectly in the form of alveoli, with basement membranes and central lumina.

Structure. The unit of this tumor is to be regarded as the alveolus rather than the epithelial cell, although the neoplastic process resides in the lining cells.

The multiplication of epithelial cells increases the length, sometimes the depth of the lining, and frequently the lumen of the affected alveolus, all of which changes cause a greater number of sections of alveoli to appear in the field. Usually lateral sprouts early develop from the original alveolus, producing new alveoli, or new alveoli develop from the downward growth of proliferating surface epithelium. In papillary and cystic adenoma there may, however, be no new alveoli formed, while lateral pouches may develop in inflammatory glandular hyperplasia. The essential process in adenoma must therefore be regarded as the neoplastic hyperplasia of the epithelial cells.

Alveoli which are elongated and pouched become variously twisted, producing circumscribed tumors differing slightly in structure from the normal gland. **(Simple adenoma.)**

Alveoli which are widened, principally by the excessive growth of epithelium into the lumen, and by retained secretion, produce the **papillary adenoma** and the **cystic adenoma.**

Alveoli in which the depth of cells is much increased produce as a rule rather malignant growths capable of infiltrating surrounding tissues and called **malignant adenoma** (*adenoma destruens*).

Adenomatoid Inflammatory Hyperplasia.

In mucous membranes which are the seat of chronic catarrhal inflammation there is frequently a development of stroma and especially of glandular alveoli which it is very difficult to distinguish from true adenoma by either gross or microscopical examination.

Unquestionably some of these inflammatory hyperplasias pass into true progressive neoplasms but others dis-

appear when the irritation causing them is removed. It is of prognostic importance to distinguish such conditions from tumors. The inflammatory hyperplasias usually exhibit little or no anaplasia but, rather, metaplasia of cells, i.e., columnar cells change to cuboidal, or cuboidal to squamous, but they fail to show the abundance of nuclear chromatin seen in tumor cells; their arrangement is more orderly than in adenoma, although it is claimed that papillary projections may develop; the process is less circumscribed than is usual with adenoma; there is usually a recognizable inflammatory hyperplasia of the stroma; and, clinically, a removal of the irritant is followed by subsidence of the hyperplasia. These conditions occur principally in the nares, uterus, rectum, and prostate.

(1) **Simple adenoma.** This is a common tumor of the breast, ovary, liver, kidney, and mucous membranes. It is usually circumscribed and often polypoid. The cells show slight anaplasia, but are often smaller and more numerous than in the normal alveolus.

They commonly retain much of their original function. The membrana propria is intact, vessels and nerves are sufficiently provided, and the supporting connective tissue is normal, or if excessive, the tumor is called *fibro-adenoma.* Lateral pouches sometimes develop from the elongating alveoli, especially when the lumen is moderately widened (*tubular adenoma*).

(2) **Papillary adenoma.** An excessive growth of epithelium may lead to a protrusion of the epithelial layer into the lumen, followed or not by vascular connective tissue papillæ. Dichotomous branching of these papillæ may lead to extreme dilatations, and complex figures on section. Retention of secretion commonly aids the dila-

multiple nuclei, which possesses ameboid properties (*the syncytium*), and (2) an inner layer of small cuboidal cells (*Langhans' layer*).

Both layers, but especially the syncytium, are concerned in the tumor.

The cells of the tumor are mostly large protoplasmic masses with numerous nuclei, possessing ameboid properties, and accompanied by a smaller number of cuboidal cells. These cells often surround new blood sinuses and exhibit a special tendency to invade the lymph or blood vessels of the uterine wall, through which widespread metastases rapidly develop. The tumors first appear as multiple, circumscribed, soft, bleeding outgrowths on the uterine mucosa, or as a diffuse infiltration of the uterine wall. They frequently develop from hydatid moles.

TUMORS OF COMPLEX ORIGIN.

Many of the sarcomata and endotheliomata show more than one type of tissue, as indicated by the terms chondro-sarcoma, osteo-sarcoma, lipo-sarcoma, chondro-endothelioma. These tumors illustrate the ordinary metaplasia of such cells and are not included in the group of tumors of complex nature.

Definition. When a tumor exhibits two or more varieties of tissue not closely related genetically or in structure, it is called a complex tumor.

Such neoplasms result from misplaced complex masses of embryonal tissue.

Varieties.

There are two classes. (1) **The Dermoid,** and (2) **The Teratoma.**

(1) **The Dermoid.**

Dermoids are complex tumors composed of skin and its appendages. These tumors are seen chiefly in the ovary, testicle, brain, and orbit. They are usually cystic. The ovarian dermoids are lined by stratified squamous epithelium from which develop hair and teeth, while the cyst is filled with sebaceous material and epithelial scales.

(2) **The Teratoma.**

A teratoma is a complex tumor exhibiting a greater variety of tissues than the dermoid, including skin and its appendages, glands, fat, muscle, nerves, and often considerable portions of organs, as the intestine, and central nervous system.

There appear to be many gradations between the teratoma and the higher distinct parasitism of one embryonic fœtus in another. Teratomata are most frequent in the sacral region, uterus, and testicle.

ROONEY AND OTTEN
PRINTING CO.
NEW YORK

Date Due

FEB 3 [illegible]			
[illegible] 21 [illegible]			
OCT	1 2 1945		

RD651 Ew52
Ewing
Syllabus of lectures on tumors

COLUMBIA UNIVERSITY LIBRARIES (hsl.stx)
RD 651 Ew52 C.1
Syllabus of lectures on tumors.
2002266393